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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,293	09/01/2000	Leandro Christmann	AVI-005	5636

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,293	CHRISTMANN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,36-39,41-49 and 51-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,36-39,41-49 and 51-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment to the claims, filed 2/2/05 is proper and entered. Claims 1-33, 40, 50 are cancelled. Claims 34, 39, 41, 42, 44-48, 53-56 are currently amended. Claims 57-58 have been added. Claims 34, 36-39, 41-49, 51-58 are pending and under current examination. Applicants' Remarks, filed 12/27/04, have been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34, 36-39, 41-49, 51-58 are rejected under 35 U.S.C. 112, first paragraph, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection that is maintained for reasons of record advanced on pages 2-4 of the prior Office action, mailed 8/25/04.

Applicants argue that the invention, as presently claimed, is fully disclosed by the specification, and point to specific support for this. See p. 5, paragraphs 2-5 of the Response.

This is not found to be persuasive. Particularly, the claims are directed to methods of enucleating a cell utilizing light in the near infrared region. These claims constitute new matter because they are not the specifically contemplated invention supported by the disclosure. The Examiner agrees that the literal support for this limitation is found in the specification, but that only in the context of using this procedure in methods of nuclear transfer. Thus, because the instant specification only teaches using TPLSM in methods of nuclear transfer, and particularly to produce donor cells for nuclear transfer methods, the claims fail to find support in the disclosure as filed. This is because the invention contemplated by the instant specification because the only contemplated invention supported by the specification is methods of nuclear transfer in avian utilizing TPLSM to produce enucleated avian oocytes.

To the extent that the claimed methods are not described in the instant disclosure, claims 34, 36-39, 41-49, 51-58 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claims 34, 36-39, 41-49, 51-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The

claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. See MPEP § 2163.06.

The newly amended limitation of visualizing internal structure of a cell utilizing light in the near infrared region and ablating the nucleus of the cell is not described in the specification. Applicants do not point, in their Response, to where specific support for this limitation can be found in the disclosure as originally filed. The specification teaches that TPLSM is used to visualize the nuclear structures in the recipient cell, and that following visualization, the cell is enucleated, optionally with two-photon laser mediated ablation, to provide a recipient oocytes. See p. 10, lines 3-6. The specification teaches that TPLSM can be used for enucleation (p. 14, line 1) and visualization (p. 19, lines 8-9, 15-19, p. 20, lines 9-14, p. 21, lines 7-12). The specification provides description for utilizing TPLSM, which utilizes near infrared light in the context of a microscope, for visualization of the recipient cell, but there is no support in the disclosure for utilizing light in the near infrared region (absent in the context of TPLSM) in order to visualize a recipient cell.

MPEP § 2163.06 further notes, "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved.

Applicant should therefore specifically point out the support for any amendments made to the disclosure."

To the extent that the claimed methods are not described in the instant disclosure, claims 34, 36-39, 41-49, 51-58 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claim Rejections - 35 USC § 112

The prior rejection of claims 34, 42, 44-47 under 112, 2nd paragraph, is withdrawn in view of Applicants' amendments to the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Response to Arguments

Applicants argue that König (1995 and 1996) does not anticipate the claimed invention because the claimed invention relates to the specific targeting of the

nucleus for ablation, and point to the specification for this support. Further, Applicants argue that targeting the nucleus for ablation is different than damaging the cell so it is unable to divide, as described by König. Thus, the present invention is not directed to damaging the cell, but specifically to the ablation, or removal, or the nucleus, and thus, Applicants submit that König cannot anticipate the claimed invention. See p. 6, 4th ¶ of the Response.

Applicants' arguments have been considered, but are not found to be persuasive. The claims require that the cell be enucleate, and this is achieved by ablation of the cell. There is no specific recitation in the claims that the nucleus be physically removed, for example. The claims to not require targeting of the nucleus for ablation. The specification supports that nuclear transfer requires the destruction or enucleation of the recipient cell before the donor nucleus can be introduced. See p. 21, lines 13-14. Applicants' method does not physically remove the nucleus, but ablate it by laser power.. Thus, the "enucleation" of a cell encompasses mechanically removing the nucleus, or destroying the nucleus such that a donor nucleus could then be introduced, in methods of nuclear transfer. Accordingly, König anticipate the claimed invention because they teach a method that fulfills each limitation of the claims, and result in a cell that cannot divide, which is results in the functional ablation of the nucleus of the cell. Finally it is noted that König teach a method using a wavelength that is within the range of that of the instantly claimed invention (see claim 38, 700-1000 nm), therefore,

because they fulfill each limitation of the claims, they would inherently produce a cell that is enucleated.

Claims 34, 36-39, 41 and 48, 49, 51 and newly added claims 57-58 are rejected under 35 U.S.C. 102(b) as being anticipated by König *et al.* (cited previously). This rejection is maintained for reasons of record advanced on pages 5-6, of the prior Office action, mailed 8/25/04.

König compare the cell damage on optically trapped motile human spermatozoa trapped by near-infrared microbeams with trapping effects at 760-800 nm compared to a continuous wave Ti:sapphire laser coupled to a fluorescence microscope. See p. 20, 1st column, 2nd ¶. The cells showed damage at 636 nm, see Figure 1 and p. 20, 2nd column. König state that the cloning efficiency of Chinese hamster ovary (CHO) cells was tested and that cells irradiated at 760 nm were unable to form clones. See p. 21, 1st column, 2nd full ¶. König conclude that continuous-wave near-infrared microbeams can cause membrane permeability, change cloning efficiency, and induce UVA-like stress (p. 21, col. 1-2, bridging ¶].

Note that the cell damage described by König is sufficient to anticipate the claims because the cells are unable to divide, which would constitute ablation of the nucleus and thus fulfill the limitation of ablation of the nucleus and the subsequent enucleation of the cell. König anticipate the claimed invention because they teach visualization of a cell utilizing a two-photon microscope within the range required

by the claim [700-1000 nm] and that human spermatozoa and CHO cells incurred cell damage. Accordingly, because König teaches the steps required by the claims, they anticipate the claimed invention.

Claims 34, 36-39, 41 and 48, 49, 51 and newly added claims 57-58 are rejected under 35 U.S.C. 102(b) as being anticipated by König *et al.* (cited previously). This rejection is maintained for reasons of record advanced in the prior Office action, mailed 8/25/04.

König teach that near infrared laser radiation may induce cell damage. They teach that near infrared trapped sperm with exposure of less than 800 nm induces UVA-like biological effects, particularly oxidative stress, and particularly that sperm trapping at 760 nm caused cell paralysis and cell death at longer exposures. See Abstract. König teach that spermatozoa subjected to 760 nm traps caused reduced motility, paralysis and loss of viability. See Table 1 and p. 2163, col. 1-2, bridging ¶. König teach that optical traps at the short-wavelength part of near-infrared spectral region can cause cell damage and cell death. See p. 2164, 1st ¶.

Accordingly, König anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-47 and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell *et al.* when taken with König *et al.*, and further in view of Squirrell *et al.* This rejection is maintained for reasons of record advanced on pages 7-9 of the prior Office action, mailed 8/25/04.

Applicants argue that there is no motivation to combine the references, as Campbell teach the reconstruction of mammalian embryos, König discuss the effects of photostress during the micromanipulation of gametes, and Squirrell teach the

dynamics of mitochondrial distribution in hamster embryos and other aspects of three-dimensional cytoarchitecture in highly photosensitive specimens, such as mammalian embryos. Applicants argue that the Examiner does not specifically point to what, in the art, would provide sufficient motivation for the skilled artisan to combine these references. Applicants argue that that further, even if a reasonable expectation of success existed, all of the limitations of the present claims are not present in the cited references, for example, specific ablation of the nucleus using laser light, or by light energy provided by the microscope.

Applicants' arguments have been considered but are not found to be persuasive. In particular, there is sufficient motivation to combine the references because Campbell provides a method of nuclear transfer, wherein the enucleation of the recipient cell can be performed by any means. See p. 5, lines 14-16. Furthermore, Squirrell teach methods to image hamsters using TPLSM, and König provide a specific method, using near-infrared microbeams to ablate a cell nucleus. The Examiner is unaware of what limitations are not taught or suggested by the prior art of record, because the art, as instantly combined, fully supports and provides sufficient motivation, for the claimed invention.

Campbell teach teaching the reconstitution of an animal embryo by transfer of a diploid nucleus in an enucleated oocyte or to a fertilized one-celled zygote that has had both pronuclei removed [see p. 2, lines 7-16]. They teach that these methods of nuclear transfer can be used in all animals, including birds such as

domestic fowl. See p. 5, lines 14-16. They teach that the recipient cells that can be used can be enucleated by any means, such as physical, actual removal of the nucleus, pro-nucleus, or metaphase plate (depending on the recipient cells) or functionally, for example by UV radiation or another enucleating influence. See p. 10, lines 12-16.

Campbell do not teach the specific enucleation of an oocyte by methods of two-photon laser scanning microscope. However, prior to the time of the claimed invention, Squirrell teach the use of two-photon laser microscopy at 1047 nm and 13 mW to image mammalian (hamster) embryos, and that by utilizing TPLSM, the embryos maintained developmental competence, as evidenced by the production of three near-term golden hamster fetuses and one live golden hamster pup. See p. 765, 2nd column, 1st ¶ and Figure 3. König compare the cell damage on optically trapped motile human spermatozoa trapped by near-infrared microbeams with trapping effects at 760-800 nm compared to a continuous wave Ti:sapphire laser coupled to a fluorescence microscope. See p. 20, 1st column, 2nd ¶. The cells showed damage at 636 nm, see Figure 1 and p. 20, 2nd column. König state that the cloning efficiency of Chinese hamster ovary (CHO) cells was tested and that cells irradiated at 760 nm were unable to form clones. See p. 21, 1st column, 2nd full ¶. König conclude that continuous-wave near-infrared microbeams can cause membrane permeability, change cloning efficiency, and induce UVA-like stress (p. 21, col. 1-2, bridging ¶) that results in the ablation of the nucleus. Thus, König provides a

methods for the visualization and conditions that result in the nuclear ablation of a cell. Moreover, König provides the conditions necessary to practice the claimed method in embryonic cells.

In view of the combined teachings of Campbell, Squirrell and König, it would have been obvious for one of ordinary skill in the art to enucleate an oocyte by visualization and ablation of the nucleus utilizing TPLSM, with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to enucleate oocytes utilizing TPLSM because Campbell teaches enucleation of the oocytes by any means to produce oocytes for nuclear transfer, and Squirrell and König teach that TPLSM, can be used to both visualize and ablate the nucleus of a cell.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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